

What's in Your Blood?

The Ongoing Hunt for Metabolites

At any given time, blood circulating through your body carries thousands of small molecules known as “metabolites.” Medical and nutrition researchers are eager to discover more about these compounds—amino acids, sugars, fats, and more—that are formed in and by our bodies.

Metabolites are of interest because the presence and concentrations of some of them can provide meaningful profiles, sometimes referred to as “metabolic signatures” or “fingerprints.”

In the future, for instance, your metabolic fingerprint—detected in a small sample of blood taken for your annual physical examination—might prove to be a reliable indicator of your health and a predictor of certain diseases. This information could then be used to create personalized recommendations about what you should eat for optimal health.

In another futuristic scenario, scientists specializing in the field of nutritional

metabolomics might use metabolic fingerprinting to assess whether experimental diet- and physical activity-based strategies can prevent the onset of disorders such as type 2 diabetes or cardiovascular disease.

Medical and nutrition researchers who are investigating serum metabolites for these and other promising applications have a remarkable new resource for their studies.

And it's only a mouse click away.

It is the Serum Metabolome database (www.serummetabolome.ca), a comprehensive, first-ever public catalog of 4,229 metabolites in human serum.

A team of 24 researchers in Canada and the United States—including Agricultural Research Service investigators John W. Newman and Theresa L. Pedersen—participated in this international project. Newman, a chemist, and Pedersen, a support scientist, are with the ARS Western Human Nutrition Research Center in Davis, California. Newman is also an

associate adjunct professor of nutrition at the University of California-Davis, where the center is located.

The ARS team and scientists at five other centers each used different analytical techniques, or “platforms,” to examine blood samples from healthy adult volunteers and from adults with cardiovascular disease.

Several Significant Firsts

Most of the metabolites documented in the database are not new to science. Nonetheless, the database represents several important firsts.

To begin with, it documents an estimated 84 percent of human serum metabolites. As such, it “represents the most comprehensive coverage of serum metabolites ever offered, in one convenient, reliable resource,” says Newman.

What's more, the database pulls together information on serum metabolites not only from the participating labs, but also from an impressive array of sources in the scientific literature—more than 2,000 in all. Careful review of these sources led to the addition of nearly 700 metabolites to the database, augmenting those detected and quantified in the laboratory analyses.

The sources were gleaned from the project's computer-assisted data mining of some 19 million scientific abstracts.

An additional first: The database is the most extensive electronically searchable compendium available today of the human



ARS nutrition researchers are analyzing the metabolites in the liquid component of blood.

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serum metabolome. This search capability greatly speeds and simplifies its use by researchers worldwide.

The database lists the detected metabolites and, if known, their association with diseases. The quantities, or concentrations, of metabolites are presented as ranges that encompass the values determined during the study and values from the curated literature.

Analytical Methods: How Do They Compare?

The project “presented an invaluable opportunity to learn more about the strengths and shortcomings of various analytical platforms by comparing the metabolite coverage and values obtained from each,” says Newman.

Five different analytical approaches were used in the project. Newman’s team worked with two: UPLC-ESI-MS/MS (ultra-performance liquid chromatography-electrospray ionization-tandem mass spectroscopy) and GC-MS (gas chromatography-mass spectroscopy).

His lab’s analyses focused on lipid metabolites involved in regulating biological processes. These metabolites are formed by the body from the fats and oils in foods such as nuts, dairy products, meats, and fish. According to Newman, regulatory lipid metabolites “are numerous, and they play important roles in tissue growth and repair, blood clotting, inflammation, pain perception, and appetite regulation. They are critical to our health.

“Our targeted analyses of these metabolites provided a swath of coverage that the other platforms used in this study didn’t capture,” he says. “In particular, more than 80 percent of the metabolites found on our UPLC-ESI-MS/MS platform were not detected by the other techniques.”

He says that the study “provides a strong starting point for determining the best future combinations of various analytical platforms to achieve maximum coverage of the serum metabolome. We know that some metabolites can be measured on multiple platforms and that different platforms have different advantages. Some are less expensive, while others are more sensitive, for example. We think our comparisons of results from different approaches will

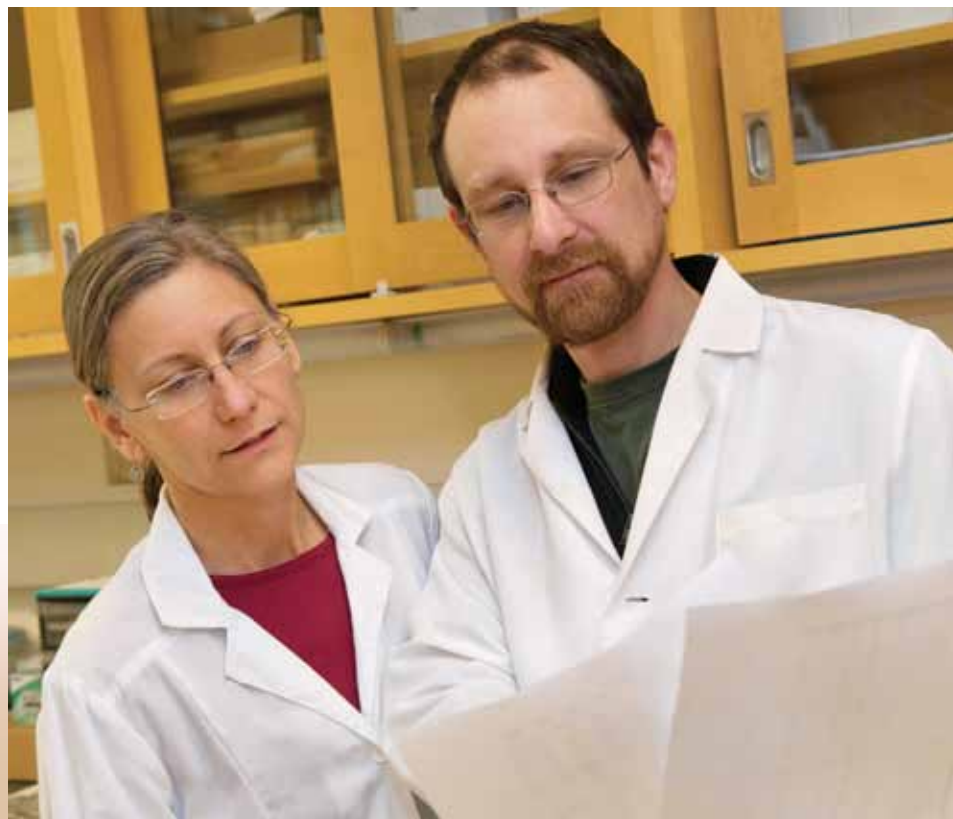
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help researchers select analytical tools in the future.”

Newman and his team are international authorities on nutritional metabolomics and the use and improvement of advanced technologies to detect and accurately quantify lipids in blood, tissue, food, and other materials. His group is interested in determining how the kinds and concentrations of lipids in our bodies are influenced by our eating habits, physical activity patterns, and genetic and environmental factors and the relation of these lipids to obesity and its adverse effects on health. The serum metabolome is, not surprisingly, a perfect tool for these investigations.

Researchers John Newman and Theresa Pedersen review a summary of lipid metabolites in blood. Our bodies form these metabolites from fats and oils in foods such as nuts, dairy products, meats, and fish.



A peer-reviewed article, published in 2011 in *PloS One*, documents the serum metabolome project. The research was led by David S. Wishart, who is with both the University of Alberta and Canada’s National Institute for Nanotechnology.

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The endeavor is part of the ambitious Human Metabolome Project, also led by Wishart, which aims to document all of the metabolites in our fluids and tissue.—By **Marcia Wood**, ARS.

This research is part of Human Nutrition, an ARS national program (#107) described at www.nps.ars.usda.gov.

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